



Unexpected Effect of Parvovirus B19 Infection on Hematological Parameters in Individuals with Normal Hemoglobin Variant

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ABSTRACT

Objectives: To assess the effect of parvovirus B19 infection on blood counts, particularly hemoglobin, and reticulocyte count, in individuals with normal hemoglobin variants.

Methods: study group, 100 individuals, is recruited from Basra Center for Hereditary Blood Diseases and Premarital Clinic in Al-Sader Teaching Hospital. Those individuals have normal hemoglobin HPLC and/or capillary electrophoresis. The samples are tested for parvovirus B19 using serological and molecular methods. Analysis of the data obtained was made by using SSPS software version SPSS 24. *P*-value <0.05 were considered statistically significant.

Results: unexpectedly significant anemia is detected in as many as 34% of those who have parvovirus infection by PCR compared with those who do not. Serological studies, although they show good concordance with PCR results, are much less sensitive and may not be helpful in the detection of acute infection. The presence of specific IgG antibodies is not protective against re-infection or activation of an already existing one.

Conclusion: Parvovirus B19 infection should be considered in any patient who has unexplained low Hb, even if he/she has a normal hemoglobin variant.

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INTRODUCTION

Human parvovirus B19 (B19V) is a single-stranded DNA virus that replicates primarily within the erythroblasts in the bone marrow, and it's been shown to persist life-long in many different cell types throughout the body following acute infection¹. Infection with B19V may cause no clinical manifestation or be associated with mild clinical syndromes, e.g., erythema infectiosum. In patients with reduced red blood cells (RBC) survival, it can cause aplastic crisis with severe anemia. Less common clinical manifestations include

arthralgia, skin rash, neurological syndromes, cardiac syndromes, and various peripheral cytopenia owing to bone marrow (BM) suppression.^{1,2}

B19V transmission may be via respiratory droplets, vertical transmission of mom to the fetus, or via the receipt of B19V-contaminated blood or blood products (e.g., packed red cells, plasma, or platelets).³

Aims of The Study

- To estimate the prevalence of B19V infection in individuals approaching medical facilities for screening purposes.

Table 1: Main instruments and analytic kits used in the research.

No.	Item	Details	Manufacturer
1	Fully automated 5-part hematology analyzer	Sysmex XN350	Sysmex, Japan
2	Hemoglobin HPLC	Variant II Hb testing system	Biorad, USA
3	Capillary electrophoresis	Capillarys system	Sebia, France
4	Thermocycler PCR	Biometra	Analytik-Jena, Germany
5	Electrophoresis system	Molecular application	Fisher scientific, USA
6	ELISA reader	Plate reader	Mindray, China
7	DNA extraction	ReliaPrep™ Blood gDNA Miniprep System kit	Promega / USA
8	Primers		Macrogen, Korea

Table 2: Hematological parameters in PCR+ vs PCR- samples.

Parameters (Mean ± SD)	PCR	Control	P-value
Reticulocyte (x10 ⁹ /L)	-	70 ± 44	0.0001
	+	15±3.7	
HGB (g/dL)	-	12.3±1.3	0.001
	+	10.1±0.2	
Platelet (x10 ⁹ /L)	-	314±95	0.135
	+	300±137	
Neu (x10 ⁹ /L)	-	4.3± 1.5	0.033
	+	5.1±1.3	
Lym (x10 ⁹ /L)	-	3.2±1.6	0.523
	+	3.1±0.9	
Mon (x10 ⁹ /L)	-	0.69±0.2	0.001
	+	0.64±0.2	

- To assess the hematological parameters in those individuals (positive or negative for B19V).
- To evaluate different B19V detection methods.

MATERIALS AND METHODS

Subjects are recruited from the premarital clinic in Al-Sadr Teaching Hospital and Basra Center for Hereditary Blood Disorders between March and December 2018, ranging from 1 year to 47 years. Those tested normal by hemoglobin HPLC and/or capillary electrophoresis, with hemoglobin (Hb) level of 10 g/dL or more, are selected. In addition to thalassemia and hemoglobinopathies, disease state or trait, and all those with significant medical illnesses are excluded.

Blood samples, 3 mL, are collected in EDTA tubes. Fully automated 5-part-differential hematology analyzers do first complete blood count. Then samples are subjected to hemoglobin (Hb) high-pressure liquid chromatography (HPLC) or capillary electrophoresis. The remaining whole blood is centrifuged to get a plasma sample for serological studies and molecular diagnosis. Plasma samples are stored at -40°C until processing.

Anti-B19V IgG and IgM are detected using ELISA method. The molecular study is started with DNA extraction, then

amplification by nested PCR of two DNA fragments of B19V in the overlapping region common to the minor (VP1) and major (VP2) capsid protein genes Yamakawa *et al.* 1995.⁴

RESULTS AND DISCUSSION

The 100 individuals recruited in this study were 49 males and 51 females with age range 1–50 years; about half of the sample is less than 10 years old.

Upon testing for B19V IgG and IgM antibodies, 77 samples (77%) are positive for IgG, while only 8 (8%) are positive for IgM. A positive IgM result, in the presence or absence of IgG antibodies, reflects an acute infection; and a positive IgG result in the absence of IgM antibodies is indicative of past B19V infection (Al Atbee *et al.*,2021).⁵

Molecular method, nested PCR, has successfully detected viral DNA in 15 (15%) samples. That means the serological method (anti-B19V) detected about 53% (8/15) of the supposed to be actual, current infections by PCR. Interestingly, all those who are positive for PCR are also positive for IgG anti-B19, suggesting that those individuals have the previous infection with the virus and got re-infection or reactivation. Hence, IgG anti-B19 Ab gives no lasting immunity against the virus.

The effect of infection on the hematological parameters can be noted clearly in Table 2. Hemoglobin and reticulocyte count show a highly significant reduction in PCR+ samples compared to PCR- samples. This reflects erythropoiesis suppression induced by B19V.^{6,7} However, other hemopoietic elements were also reduced, but the reduction was less significant.

CONCLUSIONS

Infection with B19V can cause significant anemia with reticulocytopenia in individuals with normal hemoglobin variants and are not carriers for the Beta-thalassemia trait. Considering the exclusion criteria 10 g/dL Hb level in the study sample, lower values may be expected, necessitating a survey for B19V of any patient with unexplained anemia. Serological methods, particularly IgM anti- B19V Ab, can be helpful; but with much lower sensitivity than molecular methods. Since B19V DNA can remain for a long time, possibly years, integrated within peripheral blood leukocytes after acute infection, molecular detection should be strictly confined to serum or plasma samples to detect an acute infection.

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